#15/58
9-2303

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Babak NEMATI	Art Unit: 3763
Application No.: 09/777,639	Examiner: M. Hayes
Filed: 7 February 2001	Atty. Docket: P66960US1
For: METHOD AND APPARATUS TO ENHANCE OPTICAL TRANSPARENCY OF BIOLOGICAL TISSUES	

DECLARATION OF BABAK NEMATI UNDER 37 C.F.R. 1.132

Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

In support of the accompanying response to the May 14, 2003 Office Action in the above-referenced matter, I hereby declare as follows:

1. My name is Babak Nemati. I am the inventor of the presently claimed invention. In 1990 I received a Bachelor of Science and a Bachelor of Arts degree in Mathematics and Physics, respectively; in 1991 I received a Master of Science degree in Electrical Engineering (emphasis in Applied Optics); and in 1995 I received a Ph.D. in Electrical Engineering (emphasizing Applied Optics), all from the University of Texas at Austin. Currently, I am the founder and president of Strategic Intelligence, a healthcare technology management consulting firm, and have served as a member of the boards associated with Optiscan Pty. Ltd., Plebys International, LLC, and the Lawrence Livermore National Laboratory. As further detailed in my *curriculum vitae*, attached hereto as Exhibit A, which is incorporated herein by reference, I have held management and executive positions with companies focused on healthcare, medical devices, and drug delivery.

2. I have reviewed the Office Action dated May 14, 2003, in the above matter and the present amendment to claim 70 wherein a means for applying a driving force directly contacts the surface permeability barrier and the driving force itself also contacts the surface permeability barrier. It is my opinion that a device for applying a jet injection force is positioned apart from the surface that is to receive the jet injection force. This occurs either as a function of the apparatus design, whereby a built-in spacer separates the driving mechanism from the target tissue surface, or the operational design, whereby the jet injector device does not contact the target tissue. See, for instance, the product from PenJect, Inc., at http://www.penjet.com/pages/specifications.html. The animation at that site illustrates the "operation" design, in that the pressurized gas/drug

mixture is launched at a distance from the point of contact, and the mechanism advances to come all the way up to the tissue surface. The BioJect, Inc., product illustrated in the animation provided at http://www.bioject.com/all3.html is an example of the "spacer" design. The animation at that site clearly illustrates the spacer separates the nozzle for the delivery of the gas/drug mixture, from the point on contact with the target tissue. Accordingly, it is my opinion that a jet injection device is inconsistent with the language of present claim 70.

3. I also have considered the statements by the Examiner in the same Office Action alleging that claims 72, 73, 77-84 are not patentable under 35 U.S.C. §103 because it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Edwards (US 5,833,647), Weaver (US 5,019,034), and Henry (J. Pharm. Sci. 87(8):992-925), respectively, in the method of Chan (US 6,275,726) in order to effectively delivery an agent, fluid, or molecule past a barrier tissue. More particularly, the Examiner states:

> "...all the references are concerned with methods to bypass the barrier layer of skin to deliver agents to covered tissue. The references show that it is well known in the art to use different methods to achieve this delivery. One of ordinary skill in the art would know by these references of the availability and desirability of the different methods, each having its own benefits." (page 4, second paragraph of Office Action)
> and
>
> "... all the references are concerned with the same problem of delivering agents across the skin barrier and the various methods recited in the claims are shown to be well known established methods of delivering agents to covered tissue." (page 4, third paragraph of Office Action)

4. I have reviewed the references cited by the Examiner and, as discussed more fully below, it is my opinion that (a) the drug delivery problems to be solved by Edwards, Weaver and Henry are different than the tissue transparency problem addressed by Chan, (b) one of ordinary skill in the art would not have had sufficient knowledge in these disparate arts at the time of my invention to be motivated to combine art related to systemic drug delivery with art directed to delivery of an agent for local, temporary enhancement of optical transparency, and (c) even if one did make the combination, there could be no reasonable expectation that use of the systemic drug delivery methods of Edwards, Weaver and Henry would successfully achieve local delivery of an optical enhancing agent disclosed by Chan, at sufficient volume and for a sufficient length of time to effect a meaningful (therapeutically or diagnostically relevant) change in the optical transparency of the target tissue

5. Chan addresses a different problem than Edwards, Weaver, and Henry. The Chan disclosure is focused on delivering replacement fluid to a target tissue (e.g., skin) covered by a barrier (e.g., stratum corneum) for the purpose of temporarily

increasing the light transmission through the skin. In contrast, each of the Edwards, Weaver, and Henry art cited in combination with Chan focuses on systemic delivery of therapeutic agents for a medicinal effect. Some of the differences between Chan and Edwards, Weaver and Henry are summarized below:

ELEMENT OF COMPARISON	CHAN	EDWARDS	WEAVER	HENRY
Agent to be delivered	Replacement fluid (to effect transparency)	Drug	Drug	Drug
Barrier to be crossed	Stratum corneum	Hydrogel	None	Skin
Target site of delivery	Interstitial space	Blood circulation	Blood circulation	Blood circulation
Purpose of delivery	Optical transparency	Therapy	Therapy	Therapy

In my view, the Edwards, Weaver, and Henry disclosures describe methods to systemically deliver a therapeutic drug to a subject for long term medicinal effects. In contrast, the Chan disclosure focuses on methods to locally deliver a tissue transparency enhancing agent to a subject for short term optical transparency effects. Thus, in my opinion, the problems to be solved by Edwards, Weaver, Henry and Chan are not the same. To the contrary, the problems associated with delivering a drug to a subject to achieve a systemic effect are substantively different than those associated with delivering a transparency enhancing agent to a local tissue site in a subject to achieve a transient effect.

6. Lack of motivation to combine references. My training and professional experiences in the healthcare, medical device, and drug delivery industries has provided me with exposure and, subsequently, expertise, in various areas. For instance, I have been able to combine my interests in applied optics and lasers with my interests in ophthalmology, electrically-assisted drug delivery and other applications. It has been my experience that an individual having ordinary skill in the field of transdermal drug delivery is unlikely to also have ordinary skill in the field of lasers and optics, especially as applied to methods of enhancing tissue transparency. There is little cross-over between these fields and I have rarely encountered individuals having expertise in both areas. Accordingly, it is my opinion that one of ordinary skill in these separate arts would not have had sufficient knowledge of the benefits of combining aspects of one art with the other at the time I made my invention and, thus, would not have been motivated to combine the Chan disclosure with any of the Edwards, Weaver, or Henry disclosure. This opinion is strengthened by my view, outlined above, that the problem to be solved in the Chan disclosure is substantively different than any of the problems to be solved in the Edwards, Weaver, or Henry disclosure.

7. No reasonable expectation of success if references were combined. The presently claimed invention recites a method for delivering an effective amount of a clarifying agent locally to the interstitial space of a target tissue to transiently enhance the transparency of the tissue at the delivery site. The Edwards, Weaver, and Henry disclosures are directed to delivering drug through skin or hydrogels for eventual action throughout the body (i.e., systemic action). It is my view that none of Edwards, Weaver, or Henry discloses how to deliver a drug (let alone an optical enhancing agent) to a target site such that an effective amount will be retained locally at the target site to have the desired transient effect. Therefore, it is my opinion that even if the references were combined in the manner suggested by the Examiner, none of the combined teachings would be sufficient to enable the presently claimed invention with a reasonable expectation of success.

8. I hereby declare that all statements made herein of my own knowledge and that all statements made on information and belief are true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

BABAK NEMATI, Ph.D.

Dated: September 10, 2003

EXHIBIT A TO
DECLARATION IN SUPPORT OF APPLICANT'S RESPONSE

Babak Nemati

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PROFESSIONAL EXPERIENCE

STRATEGIC INTELLIGENCE — San Diego, CA

Market-focused healthcare technology management consulting firm engaged in strategic planning, corporate development, clinical and regulatory, and product development and manufacturing consulting services

1/02 – Date ***Founder and President***

Established and conducted all aspects of SI's consulting practice. Exemplary list of consulting services include technology assessment, corporate partnering, strategic and tactical planning for commercial launch of medical device and drug-device combination products, venture development and financing services for start-up healthcare companies, and development of sales and marketing infrastructure for effective commercial launch in the US and European markets.

GENETRONICS, INC. — San Diego, CA

AMEX traded public company developing innovative therapeutic systems, based on electroporation-mediated drug and gene delivery, for applications in oncology, dermatology, cardiology, and gene therapy.

2/01 – 1/02 ***Executive Vice-President***

Directly managed corporate development and oncology marketing and sales activities of the Company, and indirectly provided strategic direction to Clinical, Regulatory, Research and Development, Engineering and Manufacturing Departments. Led all aspects of product launch efforts for the Company's proprietary surgical oncology platform technology in Europe. Secured sales and marketing infrastructure, including contract sales organizations, product distribution, servicing and support, and advertising agents across the European Union. Held expert panel meetings with surgical oncology thought leaders in Europe for market seeding of oncology products. Led financial road-shows across Europe, with interim CEO, to secure several rounds of equity financing. In the U.S. market, helped develop regulatory strategy and materially contributed to the design of the Phase III pivotal clinical protocol for treatment of head and neck cancers, that was submitted and approved by the U.S. FDA. Developed comprehensive strategic plan for partnering of Genetronics' proprietary drug-device combination products with major players in key healthcare sectors, including big pharma, specialty pharma, drug delivery companies, and major medical device companies.

8/00 – 2/01 ***Vice-President, Corporate Development.***

Led all business development and strategic planning activities of Genetronics. Defined and developed business plans for four key therapeutic fields within the Company, namely, oncology, gene delivery, dermatology and cardiovascular therapies. Identified key target companies in each therapeutic sector and forged relationships with market leaders in each field. Negotiated and closed collaborative research and licensing agreements in gene therapy with U.S. Navy, Chiron Corporation, Johnson and Johnson Research, Boeringher Ingelheim, and Valentis.

JOHNSON & JOHNSON

World's largest and most diversified healthcare company, with products in the pharmaceutical, consumer and professional market sectors, with aggregate sales of $30 billion annually.

9/99 – 8/00 ***Director, Surgical Oncology,*** **Ethicon Endo-Surgery, Inc.** Cincinnati, OH

Led the integration of an innovative drug-device combination product for localized treatment of solid tumors into the global development and commercialization processes of Ethicon Endo-Surgery. Instrumental in business planning and developing a global strategy for the growth of the newly formed oncology franchise. Devised strategies for new technology platforms to broaden product portfolio and led teams of scientists in evaluating the technical viability and market potential for new device and drug-device technologies in a broad range of oncology applications. Held expert panel meetings with thought leaders in oncology to validate clinical and regulatory strategies. Led the development of intellectual property strategy, research and development strategy, and contributed to the professional education curriculum development. Led due diligence around product and resource acquisitions.

10/98-9/99 ***Program Director, Oncology Products,*** **Ethicon, Inc.** Somerville, NJ

Global Project Leader for Ethicon's licensed electroporation platform technology for a wide range of indications in oncology. Led global clinical, regulatory, research and development, engineering design and manufacturing activities for the electroporation technology, and served a principal role in developing the strategic plan for Ethicon's global oncology franchise. Served as the key technical contact across Johnson and Johnson on the electroporation technology and established partnerships with other operating companies for pursuing the use of electroporation for gene delivery, transcutaneous drug delivery, and other non-oncology applications. Led all due diligence activities pertaining to licensing and acquisition of product opportunities in the field of surgical oncology. Served as the lead relationship manager in all interactions with our licensing partner, Genetronics. Led integration activities in transitioning the Genetronics development effort into Ethicon's global new product life cycle process. Received the *Silver Award* for leading the electroporation due diligence effort.

6/98 – 8/00 ***Chair, Global Council of Research Directors' Medical Optics Subcommittee*** New Brunswick, NJ

Founded Johnson & Johnson's first dedicated committee focused on coordination of the Corporation's activities in medical optics and leveraging the expertise and resources available across the J&J operating companies in this field. Developed a forum for technical and business exchange in Medical Optics, across the 180 Operating Companies. Organized targeted symposia for highlighting key emerging technologies of strategic interest to Johnson & Johnson. Provided recommendations for the Corporation on the merits and strategic value of key platform technologies in Medical Optics.

10/97-10/98 ***Manager, New Business Development,*** **Ethicon, Inc.** Somerville, NJ

Led identification, assessment, and licensing of new global opportunities, across a broad range of medical specialties, ranging from otolaryngology and dermatology, to surgical oncology, and assessed the strategic fit of these opportunities with Ethicon's overall growth strategy. Performed thorough business, clinical and technical assessment of new opportunities, and managed relationships with key internal and external business partners, as Ethicon's "lead contact". Served as an integral member of cross-functional teams focused on formulating strategy around new product opportunities. Presented new strategic opportunities to Ethicon's, as well as Johnson & Johnson's, corporate leadership. Led the entire due diligence process for Ethicon's licensed electroporation technology, which served as a cornerstone platform technology for Ethicon's entry into the field of surgical oncology. Received the *Silver Award* for outstanding contributions to Ethicon's global strategic planning.

5/96-10/97 **CANDELA CORPORATION** Wayland, Massachusetts

Leading manufacturer and worldwide distributor of laser dermatology and urology products (Nasdaq: CLZR).

Senior Manager, New Product Development.

Evaluated the technical and commercial viability of new product concepts, ranging from optical diagnostic systems to laser treatment modalities for dermatology and ophthalmic practices. Managed Candela's off-site clinical and pre-clinical research and development projects, and performed theoretical analysis of the underlying laser-tissue interaction mechanisms for new laser treatment modalities. Principal investigator for three SBIR projects, which received $1 million in funding from the National Institutes of Health. Managed the design, development, manufacturing, and marketing of Candela's Dynamic Cooling Device, which revolutionized laser treatment of pigmented and vascular lesions, and has since become an integral part of all laser hardware sold by Candela.

6/95-5/96 **SOMA RESEARCH CORPORATION** Austin, Texas

Comprehensive biomedical consulting firm specializing in technology development and commercialization, and market research.

Director, Technology Commercialization.

Managed Soma's consulting services for new and emerging technologies within the medical device industry. Carried out strategic technology search and identification, technology assessment, market research, product field evaluation, contract research and development, and management of pre-clinical and clinical investigations for medical device clients. Directly involved in new business development, strategic planning and administration.

3/93-4/95 **COHERENT MEDICAL, INC.** Palo Alto, California

World's leading manufacturer and distributor of medical laser products.

Consulting Project Leader.

Principal investigator for the development of the first clinically effective approach for transscleral argon cyclophotocoagulation, a laser treatment of end-stage glaucoma. Led all basic science research, pre-clinical research, and product prototyping activities.

3/92-3/93 **JOHNSON AND JOHNSON MEDICAL, INC.** Arlington, Texas

Consulting Investigator.

Co-principal investigator for the development of a *disposable* diode laser treatment system for general surgery applications. Conducted all basic science and pre-clinical research activities. Instrumental in securing intellectual property protection around research findings.

12/93-4/95 **NASA TECHNOLOGY COMMERCIALIZATION CENTER** Austin, Texas

Technology Assessment Associate.

Evaluated a wide range of technologies developed at Johnson Space Center and Ames Research Laboratory, and explored their market potential for a variety of medical applications. Assessed and developed a framework for commercialization of over 20 of NASA's most high-profile life science projects, including the NASA/Baylor axial-flow left ventricular assist device, a transcatheter system for ablation of arrhythmogenic cardiac tissues, and virtual reality systems for the rehabilitation of head injury patients.

EDUCATION

THE UNIVERSITY OF TEXAS AT AUSTIN

May 1995 **DOCTOR OF PHILOSOPHY** in Electrical Engineering (Applied Optics)
Minor in Biomedical Engineering

Dec. 1991 **MASTER OF SCIENCE** in Electrical Engineering (Applied Optics)
Minor in Biomedical Engineering

May 1990 **BACHELOR OF ARTS** in Physics *(With Special Honors)*
Minor in Electrical Engineering

May 1990 **BACHELOR OF SCIENCE** in Mathematics
Minor in Computer Science

BOARD MEMBERSHIPS

OPTISCAN PTY LTD

Publicly traded (ASX) world leader in in-vivo confocal microscopy, developed for applications in diagnostic imaging and scientific research

5/02 – 2/03 ***Advisory Board Member***

Assumed sole responsibility for the development of a comprehensive strategic and tactical plan for the U.S. launch of Optiscan's innovative diagnostic imaging platform, for applications in clinical and aesthetic dermatology, through diligent interactions with members of the Optiscan's executive management. Secured new alliances and sales and marketing infrastructure for Optiscan's entry into the U.S. marketplace.

PLEBYS INTERNATIONAL, LLC

Privately held company focused on creation, development, and growth of significant technology-based enterprises that meet underserved critical healthcare needs in global emerging markets.

3/01 – 3/03 ***Advisory Board Member***

Contributed to the development of a business plan for the newfound company for initial rounds of financing. Helped develop Plebys' strategic plan, positioning the company as a leader in the development and worldwide distribution of revolutionary healthcare technologies that meet significant unmet needs and that are beyond the reach of conventional corporate marketing and distribution efforts of multi-national corporations.

LAWRENCE LIVERMORE NATIONAL LABORATORY

U.S. Department of Energy national laboratory focused on applying science and technology in the national interest, with a focus on global security, global ecology, and bioscience.

10/96 – 1/00 ***External Advisory Board, Medical Technology Program.***

Reviewed overall strategic business plan with regards to Lawrence Livermore National Lab's technology transfer and technology development efforts in the life sciences. Instrumental in developing a strategic plan for achieving the Lab's commercialization objectives.